

ABSTRACT

A novel nuclear receptor, termed the steroid and xenobiotic receptor (SXR), a broad-specificity sensing receptor that is a novel branch of the nuclear receptor
5 superfamily, has been discovered. SXR forms a heterodimer with RXR that can bind
to and induce transcription from response elements present in steroid-inducible
cytochrome P450 genes in response to hundreds of natural and synthetic compounds
with biological activity, including therapeutic steroids as well as dietary steroids and
lipids. Instead of hundreds of receptors, one for each inducing compound, the
10 invention SXR receptors monitor aggregate levels of inducers to trigger production of
metabolizing enzymes in a coordinated metabolic pathway. Agonists and antagonists
of SXR are administered to subjects to achieve a variety of therapeutic goals
dependent upon modulating metabolism of one or more endogenous steroids or
xenobiotics to establish homeostasis. An assay is provided for identifying steroid
15 drugs that are likely to cause drug interaction if administered to a subject in
therapeutic amounts. Transgenic animals are also provided which express human
SXR, thereby serving as useful models for human response to various agents which
potentially impact P450-dependent metabolic processes.

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